UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

EXAMINER	
ART UNIT	PAPER NUMBER
	11

DATE MAILED:

This is a communication from the examiner in charge of your application
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

X Responsive to communication(s) filed on Jan. 13, 1997

This action is **FINAL**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11, 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 (three) month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133) Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) 1-45 is/are pending in the application.

Of the above, claim(s) 4-10 and 18-45 is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

X Claim(s) 1-3 and 11-17 is/are rejected.

Claim(s) _____ is/are objected to.

X Claims 1-45 are subject to restriction or election requirement.

Application Papers

X See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____

received in this national stage application from the International Bureau (PCT Rule 17.2(a))

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of Reference Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

Interview Summary, PTO-413

X Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

DETAILED ACTION

Response to Election/Restriction

1. Applicants' election with traverse of Group I, claims 1-17, and Species A is represented by claim 3, drawn to assays with NPI-1, is acknowledged. Claims 18-45 have been withdrawn from consideration as being drawn to non-elected inventions and claims 4-10 have been withdrawn from consideration as being drawn to non-elected species. Thus claims 1-3 and 11-17, as they depend from claims 1 and 2, have been examined.

The traversal is on the grounds that the groupings do not reflect distinct inventions but rather a web of knowledge which merits simultaneous examination; that the subject matter of Groups I and II do not constitute distinct inventions because the search for Group I would necessarily entail the search of Group II; that the M.P.E.P. § 803 sets forth a standard where Groups I and II should be examined together; and that even if distinct, the searches for the two Groups would not be a "serious burden". These arguments are not persuasive because, as previously explained, the searches for the three Groups are not co-extensive and would thus constitute a "serious burden" if combined.

Despite Applicants' assertions regarding the relatedness between the claimed assays, treatment methods and nucleic acids/vectors/host cells, they are nevertheless distinct inventions because they are drawn to divergent subject matter with very different components, properties, steps and uses, as explained in the Restriction Requirement of September 13, 1996. This

distinction is further supported by their separate classification (class 435, subclass 5 for Group I; class 514, subclass 12 for Group II; and class 435, subclass 252.3 for Group III). Thus contrary to Applicants' assertion, the search for Group I would not necessarily entail the search of Group II since the required classes and subclasses are not co-extensive. As explained above, if combined, these separate and divergent searches would result in a serious burden for the Examiner, and thus the Restriction Requirement is in accordance with the guidelines in Chapter 800 of the MPEP.

The requirement is still deemed proper and is therefore made FINAL.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required if the application is allowed. See PTO-948 for Draftsperson's review.

Specification

5. The specification is objected to because it does not include certain reference signs shown in the drawings. 37 CFR § 1.84(p)(5) states, "Reference signs not mentioned in the description shall not appear in the drawing and vice versa." The following reference signs are not found in the drawings: there is no Figure 2 as described on pg 4, but there are Figures 2A, 2B, 2C and 2D; there is no Figure 8 as described on pg 6, but there are Figures 8A, 8B and 8C; there is no Figure 12 as

described on pg 6, but there are Figures 12A and 12B; and there is no Figure 15 as described on pg 7, but there are Figures 15A and 15B. Correction is required.

Claim Rejections - 35 U.S.C. § 112

3. Claims 1 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed viral proteins, does not reasonably provide enablement for any viral protein "required for viral infection, replication, assembly or release". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The inclusion of claims 11-17 in this rejection is based upon their dependence from claim 1. Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claims and the unpredictability in the art.

The claims encompass assays for the identification of compounds that inhibit interactions between a host cell protein and any viral protein "required for viral infection, replication, assembly or release". Even a cursory review of viral biology, however, would find that virtually every viral protein is within the scope of that limitation because every viral "life cycle" is composed of those recited functions. Thus the claims are actually drawn to assays comprising the use of any viral protein in the binding reaction. The specification, however, only describes two influenza proteins which have been identified to bind host cell proteins. Despite knowledge in the art for the

production and testing of other viral proteins, it is *a priori* unpredictable as to which of the vast number of other untested viral proteins would bind host cell proteins. The only exception to this is in the cases where viral proteins have been found to bind cell surface proteins, such as the interactions between gp120 of HIV and CD4 of human T cells, which might be outside the scope of the claim (see rejection under 35 U.S.C. 112, second paragraph below). While recombinant techniques are available, it is not routine in the art to screen large numbers of viral protein where the expectation of obtaining similar binding activity/function is unpredictable based on the instant disclosure. Therefore, the skilled artisan would require guidance, such as information regarding which viral proteins are more likely to bind a host cell protein that is not a "cell surface receptor protein", in order to make and use proteins in a manner reasonably commensurate with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

4. Claims 1-3 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the disclosed viral and host cell proteins, does not reasonably provide enablement for any protein or peptide "corresponding to the binding site" of such proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required have been summarized above. The factors most relevant to this rejection are the scope of the claims,

unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The claims encompass assays for the identification of compounds that inhibit interactions between a host cell protein and a viral protein by use of protein fragments and mutated proteins that comprise binding sites for the interaction. The specification, however, only generally describes such assays and generic means for the production of protein fragments and mutants (pp 18-22). Despite knowledge in the art for the production of protein fragments and mutants as described, the specification fails to provide guidance regarding what fragments or mutants would be expected to comprise the necessary binding sites. It is *a priori* unpredictable as to which of the enormous number of possible fragments and mutants would retain the necessary binding sites. It is further unpredictable as to whether specific protein modifications, such as phosphorylation and glycosylation, also play roles in the protein-protein interactions required in the claimed assays. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what amino acids can be altered or removed from a protein and still result in similar binding activity/function is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements for the binding sites of both the host cell and viral proteins is lacking, it is unpredictable as to which protein fragments and mutants, if any, of the disclosed proteins retains the necessary binding activity. Moreover, it is unpredictable as to whether interactions between fragments or mutants are those that

are responsible for interactions between the native proteins. Thus the identification of compounds that inhibit interactions between two fragments does not necessarily mean that the compounds will inhibit binding interactions between the two proteins. Lastly, while recombinant techniques are available, it is not routine in the art to screen large numbers of protein fragments and mutants where the expectation of obtaining similar activity/function is unpredictable based on the instant disclosure. Therefore, the skilled artisan would require guidance, such as information regarding the location, size, and sequence of alterations in or deletions from the disclosed proteins which preserve their binding/interaction activity, in order to make and use proteins in a manner reasonably commensurate with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

5. Claims 1-3 and 11-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assays using the disclosed binding conditions, does not reasonably provide enablement for assays conducted "under conditions and for a time sufficient to permit binding and the formation of a complex". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether undue experimentation is required have been summarized above. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

The claims are drawn to encompass assays conducted "under conditions and for a time sufficient to permit binding and the formation of a complex". The specification, however, only discloses the use of conditions in a "yeast interactive trap system" where the assay occurred within yeast cells (pp 34-36). Despite knowledge in the art for recombinant expression in other organisms, the specification fails to provide guidance regarding what assay conditions are necessary or appropriate for any given protein, or fragments and mutants thereof. It is *a priori* unpredictable as to which of the enormous number of possible assay conditions would result in interactions permitting interaction between the two proteins. Since it is a priori unpredictable as to what conditions such as ionic strength, pH, molecular complexity and energy and cofactor requirements would be expected to play roles in the specific protein-protein interactions required in the claimed assays, the skilled artisan would require knowledge of and guidance with regard to which conditions, if any, to modify and which to maintain as well as detailed knowledge of the ways in which the proteins behave in each set of conditions. Since it is beyond routine experimentation in the art to attempt all possible reaction conditions with each pair of protein molecules, the skilled artisan would require guidance, beyond that provided, to make and use assays in a manner reasonably correlated with the scope of the claim. Without such guidance, the experimentation left to those skilled in the art is undue.

6. Claims 1-3 and 11-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite for recitation of the term "receptor protein" since there is no general consensus on the definition of "receptor" in the art and the specification fails to define it. For example, both Stedman's Medical Dictionary and Martin teach that "receptor" is defined as a cell component that binds to a hormone or other regulator without inclusion of binding viruses while Merriam-Webster's Medical Desk Dictionary and Henderson both include virus binding to the above definition. Since there is no art recognized definition for the term and it is part of a negative limitation in the claims that materially affects the scope thereof, the skilled artisan would be confused as to the metes and bounds of the claimed invention.

The claims are also indefinite for recitation of the phrase "amino acid sequence corresponding to" (twice in each of claims 1 and 2) because it is unclear as to the scope and breadth of "corresponding to" when used in connection with an amino acid sequence. Possible interpretations of the phrase include amino acid sequences of the same length, the same amino acid composition or the same sequence. Since all of these are reasonable and distinct possibilities with very different consequences for the claimed assays, the skilled artisan would be confused as to what amino acid sequences are actually encompassed by the claims.

Claims 2 and 3 are also indefinite for recitation of the abbreviations "NP" and "NPI-1", respectively, since alternate subject matter utilizing the same abbreviation may exist and introduce

confusion. Replacement of the abbreviations by the proteins' full names, such as "Nucleoprotein" and "Nucleoprotein Interactor-1" would obviate this rejection.

Claim Rejections - 35 U.S.C. § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 11, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Maddon et al. This rejection is based on a reasonably broad interpretation of the claims where the negative limitation comprising "receptor protein" is interpreted as having a narrow definition which excludes "receptors" that bind viruses (see rejection under 35 U.S.C. 112, second paragraph, above).

Maddon et al. teach soluble T4 (sT4) as well as some fragments thereof which are capable of inhibiting binding between T4 on cell surfaces and gp120 on viral particles. They further teach assays to determine whether sT4 inhibits the binding (see column 43, line 11 through column 44, line 16) as well as assays to determine whether sT4 fragments can inhibit gp120 mediated HIV binding (column 44, line 32 through column 47, line 30). Lastly, they teach the use of sT4 in assays to screen for inhibitors (column 9, lines 31-33). Since they teach assays where T4 is on a cell surface, gp120 is on the viral particle and detection is by labeled antibodies followed by cell sorting, they anticipate the claims.

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Gannon et al.

Gannon et al. teach assays for the inhibition of binding interactions between SV40 T antigen and eukaryotic DNA polymerase alpha and p53 (see especially pp 88-90). Since T antigen is a viral protein required for viral DNA replication and both polymerase alpha and p53 are not a "cell surface receptor protein[s]", Gannon et al. anticipate the claim.

9. Any inquiry concerning this communication or earlier communications should be directed to Kawai Lau whose telephone number is 703-308-4209. The examiner can normally be reached Monday-Friday from 7 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Wax, can be reached at 703-308-4216.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is 703-308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission to the attention of the examiner in Art Unit 1814. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (October 19, 1988) and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The FAX telephone number is 703-305-7401. Note: If applicants do submit a paper by facsimile, the original signed copy should be retained by applicants or applicants' representative. No duplicate copies should be submitted so as to avoid the processing of duplicate papers in the Office.

Kawai Lau, Ph.D.
March 10, 1997

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
GROUP 180